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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/822,186	03/20/97	RUEGER D	CRP-137

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EXAMINER	
ROMEO, D	
ART UNIT	**PAPER NUMBER**
1646	26

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary	Application No. 08/822,186	Applicant(s) Rueger et al.
	Examiner David S. Romeo	Group Art Unit 1646

☒ Responsive to communication(s) filed on *24 Jan 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-25, 31-33, 35, and 36* is/are pending in the application.

Of the above, claim(s) *1-25, 31-33, 35, and 36* is/are withdrawn from consideration, to the extent that they are drawn to a non-elected inventon

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-25, 31-33, 35, and 36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-25, 31-33, 35, and 36* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendment filed 01/24/00 (Paper No. 23) has been entered.

2. Claims 26-30 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 20. Applicant's elected without traverse OP-1, carboxymethyl cellulose, collagen, critical size defects in Paper No. 20. Claims 1-25, 31-33, 35 and 36 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b) to the extent that they are drawn to a non-elected species. Election was made **without** traverse in Paper No. 20.

3. Any objection or rejection of record that is not maintained in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 2, 3 are rejected under 35 U.S.C. 112, second paragraph, over the recitation of "conservative amino acid sequence variants". Applicants argue that it is well known in the art what a conservative amino acid substitution is. Applicants' arguments have been fully considered but they are not persuasive. It is noted that the feature upon which applicant relies (i.e., amino acid substitution) is not recited in the rejected claim(s). Although the claims are interpreted in

light of the specification, limitations from the specification are not read into the claims. The specification does not contain a limiting definition of "conservative amino acid sequence variants".

5. Claims 1-5, 7, 15, 20, 22, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato et al. (U21). Applicants argue that Sato's BMP is not equal to the purified OP recited in claim 1, and that there is not a reasonable expectation of success. Applicants' arguments have been fully considered but they are not persuasive. Sato clearly teaches purification of the BMP-iNCP (paragraph bridging pages 254-255). To the extent that the BMP-iNCP was purified then the BMP was purified. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., not associated with other osteogenic materials with which it is normally associated) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Evidence of secondary considerations, such as unexpected results, commercial success, or reasonable expectation of success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 179 USPQ 421, 425 (CCPA 1973).

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6. Claims 1-5, 7, 8-12, 15 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Kuberasampath et al. (AA). Applicants argue that the collagen-GAG polymer does not fall with in the scope of claim 1. Applicants' arguments have been fully considered but they are not persuasive. The claimed device comprises a matrix. As such, the claimed device does not exclude a matrix that is a synthetic polymer. The collagen-GAG polymer further comprises collagen. In claim 8 the matrix is collagen. Kuberasampath's device comprising collagen meets all the claimed limitations of the matrix that is collagen.

7. Claims 1, 32, 33, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath et al. (AA) as applied to claim 1 above. Applicants argue that the collagen-GAG polymer does not fall with in the scope of claim 1. Applicants' arguments have been fully considered but they are not persuasive. The claimed device comprises a matrix. As such, the claimed device does not exclude a matrix that is a synthetic polymer. The collagen-GAG polymer further comprises collagen. In claim 8 the matrix is collagen. Kuberasampath's device comprising collagen meets all the claimed limitations of the matrix that is collagen.

8. Claims 1, 13 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath et al. (AA) as applied to claim 1 above, and further in view of Wozney et al. (BE, cited by Applicants) and Amman et al. (BA, cited by Applicants). Applicants argue that the

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collagen-GAG polymer does not fall with in the scope of claim 1. Applicants' arguments have been fully considered but they are not persuasive. The claimed device comprises a matrix. As such, the claimed device does not exclude a matrix that is a synthetic polymer. The collagen-GAG polymer further comprises collagen. In claim 8 the matrix is collagen. Kuberasampath's device comprising collagen meets all the claimed limitations of the matrix that is collagen. With respect to claim 31 and the unexpected results, it is noted that at page 86, lines 3-5, it is stated that unexpectedly new bone was continuous with the host bone more frequently. With the smooth, moldable putty or paste, as taught by Ammann (page 10, line 30), one of ordinary skill in the art would have a reasonable expectation that the implant would from a more continuous layer with irregular host bone defect sites and more frequent new bone would be formed that is continuous with the host bone. With respect to claim 31 and the unexpected results, it is noted that at page 87, lines 1-7, the unexpected results were apparent at low doses of OP-1, and the generic claim is are not limited to low OP-1 doses.

9. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (U21) as applied to claim 1 above, and further in view of Wozney et al. (BE, cited by Applicants). Applicants argue that either Sato or Wozney do not teach the device of claim 1, nor do they either render it obvious or suggest it. Applicants' arguments have been fully considered but they are not persuasive. With respect to claim 1, Sato clearly teaches purification of the

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BMP-iNCP (paragraph bridging pages 254-255). To the extent that the BMP-iNCP was purified then the BMP was purified. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., not associated with other osteogenic materials with which it is normally associated) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Evidence of secondary considerations, such as unexpected results, commercial success, or reasonable expectation of success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 179 USPQ 421, 425 (CCPA 1973). With respect to claim 13, the examiner submits that Wozney's autologous blood is fibrin glue and Wozney teach the use of either autologous blood, i.e. fibrin glue, or CMC for the same purpose in order to achieve the same result. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use either autologous blood, i.e. fibrin glue, or CMC in an osteogenic device. The invention is prima facie obvious over the prior art.

10. Claims 1, 13, 17-25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (U21) and further in view of Wozney et al. (BE, cited by Applicants) as applied to claims 1 and 13 above and further in view of Doll et al. (V21), Cook et al. (CD, cited by

Applicants), Nunez et al. (BD, cited by Applicants), Amman et al. (BA, cited by Applicants), Alberts et al. (W21), and Reddi et al. (X21). Applicants argue that claim 1 is distinguished over the prior art, consequently claim 13 is also non-obvious, and for these same reasons claims 17-25, 31 are also non-obvious. Applicants' arguments have been fully considered but they are not persuasive. With respect to claim 1, Sato clearly teaches purification of the BMP-iNCP (paragraph bridging pages 254-255). To the extent that the BMP-iNCP was purified then the BMP was purified. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., not associated with other osteogenic materials with which it is normally associated) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Evidence of secondary considerations, such as unexpected results, commercial success, or reasonable expectation of success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 179 USPQ 421, 425 (CCPA 1973). Doll also teaches that collagen matrix may provide a more permissive surface for cell attachment than HA, and it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to substitute collagen for the HA in order to provide a more permissive surface for cell attachment. Cook's composite had the consistency of wet sand, which was spooned into the segmental defect site (paragraph bridging pages 303-304). It would have

been obvious to one of ordinary skill in the art at the time of Applicants' invention to add a gelling agent, such as CMC, because it the implant could be molded into the desired shape or formulated for injection. Nunez teaches that FG is a gel and that TSs such as FG can be molded into any desired shape; this cannot be done with DBM powder because DBM powder will not maintain its shape. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use CMC for forming a gel that would prevent soft tissue collapse into wound beds packed with DBM and osteogenin, and to maintain the osteoinductive properties of the implant and promote the emigration of osteoprogenitor cells into the wound bed. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to add collagen in order to provide a more permissive surface for cell attachment. Alberts teaches the physiological properties of the ECM and Reddi teaches that biomaterials mimic the extracellular matrix. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to mimic the ECM in order to achieve osteoinduction and to mimic a gel-like "ground substance" with a gel forming material, such as CMC.

11. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (U21) as applied to claim 1 above, and further in view of Ogawa et al. (U). Applicants argue that Sato does not teach the device of claim 1, and as a result the cited references do not teach the device of claim 1 or 6. Applicants' arguments have been fully considered but they are not

persuasive. With respect to claim 1, Sato clearly teaches purification of the BMP-iNCP (paragraph bridging pages 254-255). To the extent that the BMP-iNCP was purified then the BMP was purified. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., not associated with other osteogenic materials with which it is normally associated) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Evidence of secondary considerations, such as unexpected results, commercial success, or reasonable expectation of success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 179 USPQ 421, 425 (CCPA 1973). With respect to claim 6, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use TGF-β and BMP in the device of claim 1 with a reasonable expectation of success in order to achieve a synergistic promotion of bone formation.

12. Claims 1 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath et al. (AA) or Sato et al. (U21) in view of Wozney et al. and Amman et al. as applied to claims 1 and 13 above, and further in view of FMC Corporation (Y21). Applicants argue that Kuberasampath, Sato, Wozney, and Amman are not applicable to claims 1 or 13. The examiner maintains that Kuberasampath, Sato, Wozney, and Amman are applicable to claims 1 or

13, as discussed above. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to combine either CMC or MC with MCC, as taught by FMC Corp., in the device of claims 1 or 13 with a reasonable expectation of success, in order to vary the rheological properties of the device according to its desired use, such as injection.

New formal matters, objections, and/or rejections:

Claim Rejections - 35 USC § 112

13. The claims 1-6, 9-16, 32, 33, 35, 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are indefinite because it is unclear if the device comprises a matrix that is not a synthetic polymer and that is not demineralized bone, or if the device comprises a matrix other than a synthetic polymer or the device comprises demineralized bone. The metes and bounds of the claim(s) are not clearly set forth.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 6:45 a.m. to 3:15 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242.

Faxed draft or informal communications should be directed to the examiner at (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID ROMEO
PATENT EXAMINER
April 8, 2000